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THE METSCHNIKOVIAN THEORY OF VITAL RESISTANCE.

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THERE is a large and marvellously interesting class of phenomena associated with the history and sequelæ of certain of the acute zymotic diseases characterized as immunity, which has long been recognized as the possible source of a potent ally to preventive medicine providing that its subtle nature and mechanism should ever become understood sufficiently to render it susceptible of imitation and employment for the arrest and anticipation of infectious disease. The advent of vaccination as a prophylactic in smallpox was the first actual realization of what lay concealed in this direction, and its discovery gave a new importance and significance to what had hitherto been mere conjecture and speculation. Notwithstanding this fact, however, and that this great adjuvant has been usefully employed for a number of years, its underlying and mysterious principles have remained quite isolated and signally barren of generalized results applicable to other disorders of analogous characters. These failures to discover and apply the *mode* of vaccination have not, however, deterred the ambitious nor caused the speculative mind to entirely relinquish the hope of its ultimate success; but, on the contrary, the spirit of inquiry and experiment has been more or less potent all along, and is just now more vigorous than ever before. That the subtle and obscure conditions associated with and constituting the cause of immunity or vital resistance will finally be detected and opened up as a generalized auxiliary to medical art, is the ambition of many and the hope of all.

In an article with the dimensions of the present one, it is quite impossible to enumerate and discuss the several and various kinds of immunity known to exist both as natural and acquired conditions of certain organisms in relation to certain diseases, and we



shall have to limit the observations to that of the acquired form alone, which experiences show to be the result of two classes of agencies or influences; namely, immunity from a natural and immunity from an artificial attack of disease. It may be stated that it is now very generally believed that the agencies of immunity, the *vis medicatrix naturæ*, and the factors of vital resistance are one and the same, and that the special functional activities of the body-cells are the chief or sole agents in the arrest, cure, and prevention of germ disease. It is from this conception and rôle of the cells that this paper is undertaken, and its purpose will be to search out and ascertain the nature and influence of these agents and agencies, and, in so far as is possible, to assign to each its separate value and importance in the origin, manifestation, and sequelæ of infectious disease. In all sciences where the processes are imperfectly observed the theory of the process (which is a systematic survey of all the facts of the case marshalled in the order of their causal dependence) is supplemented by an hypothesis which bridges over with a guess the gap left by observation. Immunity, like a number of kindred occult subjects, has had a vast number of hypotheses and speculations to explain it, though none of these have as yet evidenced the *sine qua non* of reconciling observation with calculation to that degree which would warrant their acceptance as the true and legitimate theory of immunity. Unfortunately for medicine, in a large proportion of the explanations advanced in connection with its dark problems of disease we can never, from the nature of the subject-matter, approach nearer to a solution than what mathematicians call "a first approximation." It is through such successive approximations that all science advances; yet in the instance of a diseased organism these must ever remain somewhat of a mystery, and we can never pass to the final stages of the How and the Why.

Among the theories advanced, there is one which has recently gained considerable prominence, which may be provisionally regarded as the correct one, both from the number of facts which it explains, and also from the manner in which it has withstood the tests of experiment and criticism, though its claims are stoutly opposed in some directions. This theory, as originally propounded by its author, Metschnikoff, undertook to ascribe the chief phe-

nomena of immunity, both natural and acquired, to the functional or vital actions of the body-cells, though, as now modified by its expounders, it concedes the ancillary office of other agencies, though of a subsidiary character.

Before proceeding to a detailed consideration of this theory, it is necessary, to a clear comprehension of the issues involved, that we take a brief survey of the salient features in the genesis and life-history of the body-cells. Biology teaches that the cell is the basic element of all life. As a primitive part, it may be either an organism or an element in an organism. That it may lead an isolated life, as plant or animal, or it may become united with other cells and lead a more or less corporate existence; but always, even as an element of a higher organism, it preserves and retains its own individuality as a cell. At first we see that the corporate union is very slight, merely the contact of one cell with another of its own kind—as the filament of a conferva. Rising higher, we see the cell united with others different from it. Plants and animals appear, having structures composed of various cells. Rising still higher, we see animal forms of which the web is woven out of myriads and myriads of cells, with various cell products, processes, fibres, and tubes. Viewed in this manner, the cell is seen to be the elementary factor of life, and the complex organism is but an aggregation of these elements, though this association is not a complete subordination of living parts, but each and all are mutual and co-ordinate, and there exists an interdependence of parts in so far as every part is dependent upon every other part. Each is, so to speak, a condition of existence for every other part, and the unity of the organism is but the expression of its solidarity. This is true, insomuch that, whenever organized substances become differentiated into morphological elements,—such as cells—each of these has its own evolution, separate and distinct, and is born, lives, and dies as an individual. Hence, whether as an element or as an organism, associated or differentiated, the cell possesses and retains its own individuality, and lives as a separate creature. The vital or functional activity of the cell is of a threefold kind. It is directed in part towards its self-preservation, self-propagation, and the altering of outward relations. Virchow distinguishes these severally as the nutritive,

formative, and functional activities. Many of these functions of the cells cannot be seen, and are only known through their effects. Others, again, like motion, growth, multiplication, ingestion, and alterations in form, can be directly observed under the microscope. Every cell, whether isolated or joined with others, is influenced by the nature of its environment. This may assist or antagonize its vital functions. They may disturb to a degree amounting to a complete arrest of all the signs of cell-life, or they may accelerate them all to the highest point of activity. Let the temperature be raised, a noxious substance be present, or an enemy to cell-life approach, and there is at once a corresponding change in the behavior of the cell. The cell is autonomous in itself, and yet it is subject to its conditions of external existence. To pass further into details: All microscopists are familiar with the spectacle of a formless lump of albuminous matter (a Rhizopod) putting forth a process of its body as a temporary arm or leg, or else slowly wrapping itself around a microscopic plant or morsel of food-substance, thus converting its whole body into a mouth and stomach. These phenomena are, however, surpassed by another monad, which fastens itself to a plant and sucks the chlorophyll first from one cell and then from another, while a second monad, unable to make a hole in the cell-wall of the plant, comes along and thrusts long processes of its body into the openings already made, and drags out the remains of the chlorophyll left by its predecessors. And still another, a third monad, comes, leading a predatory life, and falls upon those who have filled themselves with food, and takes it away from them. It is here that we stand at the threshold of that dark region where animal will begins, though we are, as yet, in the presence of the lowest forms of life known to science. It is in this direction concerning the facts in the genesis, morphology, and physiology of the cell, as interpreted by the laws of development and heredity, that science looks for a solution of those questions which have hitherto baffled all efforts. To understand and to estimate their several values, and their import as factors in the conditions of immunity, is to solve the mystery and to invoke their allegiance to the medical art.

It has long been known that inert particles of matter, such as

pieces of bone, sponge, animal ligatures, and the like, when introduced into the blood and tissues of an animal, would become speedily dissolved, taken up and destroyed by the cells. The significance of these facts was first pointed out by Hæckel, who compared this process of the cells to that occurring in unicellular organisms by which they took in, digested, and lived upon lower forms of life which surrounded them. He concluded that the cells of a complex organism nourished themselves by this same means, and that they took up and digested foreign substances in the same manner as the primitive cells. In other words, he theorized that the nutritive function was the same in both, and that the lower forms were sustained through the power of attacking and devouring other microorganisms, while the higher or complex cells used this power to destroy and remove foreign substances. Carl Rosser extended these observations by the means of experiments, and demonstrated that the amœboid cells of the animal body did really possess this power of taking up and destroying living microorganisms; and, as a result of this, he drew the inference that the complex organism as a whole was protected against the invasions of pathogenic microorganisms by this function of taking up and destroying—*phagocytosis*—and that in its absence or imperfection an animal became susceptible. At this stage of the subject Metschnikoff took it up and followed the conclusions of Hæckel. He maintained with him that the power of attack as witnessed in the primitive or predatory cell had never completely declined through the ascending stages consequent upon development, but that it had remained all along, though in a latent form, since the altered conditions in its media by which the necessary pabulum for sustenance was furnished without effort upon its part, and there was no demand for this power of attacking microorganisms.

In substantiation of these views he proceeded to demonstrate that the latent or potential power of successful attack could be made patent and reinstated by suitable circumstances or exigencies rendering its operation necessary. To illustrate this he employed by means of inoculations attenuated viruses, which, through their mild, gradual, and stimulating influences upon the functions of the cells, caused them eventually to reassert their former or primitive instincts or powers of attack, and overcame and destroyed

microörganisms, which at first destroyed them. In this way he argued that the predatory function could be made to exercise itself in all its old vigor, and that by a series of gradually increasing dosage of quantity and quality the cells were drawn out, acclimated, and made superior to the microörganisms. It was from these facts in the history of the cell's life and experiments given that he formulated and advanced the theory that immunity was vital resistance whose processes were phagocytosis; that, when an organism was susceptible and invaded by pathogenic microörganisms, it was due to an absence or imperfection of this function of the cells; and when, on the other hand, an organism was refractory or exempt, it was because the cells attacked and successfully destroyed them in the beginning. This very plausible explanation, as drawn from these data, is, however, denied, and it is disputed that the cells possess and exercise this function as a means of defence in a complex organism.

Prominent among these opponents stands Klein, who, by experiments with the bacilli of tuberculosis, has shown that the cells in taking up the microörganisms are themselves destroyed, and instead of being a means of protection, it is really the reverse process of destruction. On the other hand, a number of experimenters, such as Metschnikoff, Sutton, Ruffer, and Walker, have demonstrated that the cells will take in and destroy as many as fifty living anthrax bacilli, and still continue to live and thrive. In supplement of both of these apparently discrepant observations, Roux has shown that this process of taking in and digesting microörganisms—phagocytosis—is never an absolute one, but always a relative process, capable of being modified, increased or decreased by a large number of internal and external conditions and influences affecting the body-cells; that it is always and invariably present and operative in direct ratio to the non-susceptibility of any particular organism, and that it is only complete in all its details in those perfectly refractory, while in the susceptible ones it is partial, incomplete, or even entirely absent or unavailing. Hence, it cannot be denied but that in some instances the cells are destroyed, while in others they are the destroyers. Indeed, this is true in so far that in every acute and immunizing invasion of disease there are numbers of cells de-

stroyed. On the other hand, if the organism be the superior antagonist from the very first, the microörganism fails to gain admission, and the disease is prevented. In the first of these instances, where the microörganisms enter and destroy the cells for a time, how is it possible for the latter to ever gain the ascendancy over the germs, and to cast them out, as we know they do? What is the nature of those influences and conditions by which these are effected? The theory of acclimation or toleration cannot be tenable in the case of a cell that is dead, since, as such, it has really ceased to be a part of the vital economy. *The death of the cell furnishes the key to the entire situation*, though its recognition, as such, has long been overlooked and misinterpreted. The influence and rôle of fever as a vital and conservative reaction of the organism has been long misunderstood. The discovery and employment of its principle are the most important advance which has ever been made in connection with the mechanism and rationale of vital resistance. The death or destruction of the cells does not terminate its influence upon the organism, as has been thought; but, on the contrary, in itself becomes the source and means by which changes of the first importance to the organism are originated. The death of the cell liberates its constituents or tissue extracts in the form of substances denominated variously as tissue-fibrinogen (Wooldridge); nuclein (Horbaczewski); alexin (Hankin); tuberculocidin (Klebs); and elixir-of-life (Brown-Séquard). All of these, under varying degrees of chemical purity, depending upon the processes by which they are produced, are considered to be the same or analogous substances whose several effects upon the organism are the production of intense cellular actions in the form of chemotaxis, proliferation, fibrosis, and phagocytosis.

When either of these substances is liberated in the organism by the destruction of the cells from any cause, all of the phenomena characterized as vital resistance immediately transpire. They are the most powerful cell-manure, and cause fever and intense cell-action of all kinds. Should this destruction of the cells, however, be carried beyond a certain limit, which may be designated the physiological reaction, a state of septicæmia arises from the large quantity of ptomaines present. It is under the stimulating influences of these powerful substances derived from the

destruction of the cells that the surviving body-cells are enabled to resume their latent functions—to attack the microorganisms which are attempting to destroy, and to overcome them. That these effects do follow, and that these substances do possess these properties, is now generally conceded and capable of demonstration by any one. All that is required to see the processes of phagocytosis in operation is a lens, a little frog's lymph, and some anthrax bacilli. With these the process may be watched, and the cells can be seen taking in and digesting the bacilli. With these facts we are, in a degree, prepared to comprehend the details of the processes by which the organism protects against and arrests disease. In a process so general as this one, which must necessarily go on to a greater or less degree continuously, owing to the universal presence of germs in some form or other, it is objected that the cells could never obtain a special training and be able to manifest a specific exemption, which we know is the case with a number of immunizing diseases.

After an attack of disease conferring an immunity there is an exemption from one disease alone. All theories of immunity have, as yet, rested at this particular stage of their career, and none have shown their ability to pass it and carry conviction with them. How do the body-cells receive and retain a specific immunity? As already seen, the struggle between the cells and the microorganism is between two living organisms, both possessing distinct individualities, functions, and products. The microorganisms, just as the cells, produce and liberate life-products and waste, which circulate in the tissues of their host along with those of the latter's production. Thus far the cellular activities have been attributed to those products arising from the cells alone, though in every attack of disease the phenomena must transpire in the presence of and under the influence of both of these classes of products. The products of the germs *per se*, the leucomaines, are also capable of augmenting the vital actions of the cells, acting as stimulants, and causing all the phenomena of phagocytosis; and when this passes beyond the stage of physiological reaction, the same as that produced by the death of the cells through their products, there are high fever, intense constitutional disorder, and septicæmia. Now, experiments show that it is possible to in-

duce the refractory condition from either of these two classes of substances when employed singly and alone. The tissue-juices, cell-extracts, or products—spleen, lymph-glands and testicle—when removed artificially from crushed tissues, are capable of producing, when injected into an animal, all the phenomena of vital resistance in an augmented form; and the culture-fluid products of pathogenic germs will, when injected, also bring about the same changes, both resulting in the refractory condition of that organism. In other words, that immunity communicated by the different substances and methods of preventive inoculations, or natural attacks of disease, is in reality all acquired by the same process and mechanism of the cells. Increased resistance from any cause, original or acquired, is but the expression of the augmented powers of phagocytosis of the cell. The destruction of the germ is always effected by this process, though the chemical influences of the intercellular juices and products doubtless assist to some degree. Even in natural immunity, repeated inoculations train and strengthen the cells, and make them destroy more completely (Chaveau). Ferran shows that the refractory condition becomes stronger and stronger the oftener the inoculations are used and repeated. This is true in so far that a susceptible and weak animal may be made to resist the most virulent and deadly germs. The experiments of Metschnikoff will explain the modus of these acquirements and show how any influence whatsoever, which is capable of reawakening the latent functions of the cell, may bring out and strengthen them so that an adaptation will transpire and a superiority will be the consequence.

The real effects of either of these substances will be the same, and a corresponding change in the function and structure of the cell will follow as the consequence of alterations in environment.

The laws of biology, as applied to the instances in point, show that, whenever from any causes there is an actual change in the media of an organism, there is always a reaction and consentaneous change in its structure. All structural changes find their expression in altered functions, since the function is but the directed energy of the properties of a tissue. In this way, the slightest change in the external media of a cell may give rise to the most complex results in its behavior. It may call the cell into increased activity

—increased waste and repair—and thus become the origin of the widest variation. Thus, every change of composition or constitution in the medium must find a response in the cell, and the cell becomes modified by every such response. Again, every modification must be a selection determined by the laws of growth—the affinities of the cell—and every increment of function is preceded by an increment of substance. In the naturally acquired form of immunity we have, in addition to the stimulating effects of the tissue-extracts arising from the death of the cells, also those of the specific products of the microorganisms. It is in the presence of this *specific* factor that we find the special modifications causing a particular immunity, which the cells manifest in the future. It is an element in the conditions of existence of the cells, and it must necessarily have its effects in the final synthesis and representation of an acquired immunity.

The tissue-extracts or proteids raise the physiological activities of the cells to a state of tension, so to speak, where the slightest alteration in their media would produce a change and a registration, impression or modification, in the form of increased vital resistance, which, under less favorable or imperturbing conditions, would have been unappreciated and caused no change. This feature in the history of the elementary cell finds its analogue in the well-known physiological law of complex organisms, wherein an impression or registration is always retained in direct ratio to its vividness below a certain stage incapable of actual injury to the organism. It is during this intense stage of heightened vital action that the cells are influenced by the specific factor, and it becomes indelibly impressed upon their future existence.

In this process, we understand how it is that a vaccination “takes” best and ensures the highest degree of protection when there is considerable vaccination fever. Indeed, in all successful inoculations of attenuated viruses, this reaction, either in a marked and rapid or a mild and protracted form, is considered an essential part of all experiments. That the specific substance is the cause of the specific immunity may be illustrated still further by the experiments of Emmerich, Chamberlain, Pasteur, and others, who show, that while the tissue-extracts, chemical substances, and various internal and external influences will cause all of the phenomena of

cell action, including chemotaxis, proliferation, and phagocytosis, when introduced into the tissues of an organism, yet this is only absolutely efficient or discriminative to a degree of producing complete and permanent immunity when the previous inoculations or attacks embraced the specific factor or substance of those microorganisms with which the tests were made. In other words, that the various stimulants noted would only cause an increase in the general physiological powers of the cells; but they did not manifest a special or particular form of resistance, unless the specific substance had been used.

Without multiplying examples to corroborate this position as true, we are safe in saying that the cells of the body do become modified or developed through influence of environment just as all organisms, simple or complex, and that they retain these modifications as specific changes, since life itself is but the aggregations of external and internal media.

It is now in order that we trace those circumstances by and through which the cells preserve and transmit these modifications in the form of heredity. It is not necessary or practicable in an article like this to undertake the examination of the theories advanced in connection with heredity. We shall rest with the fact that there is such a process as heredity, and not undertake to discover or discuss its philosophy. Every one who has pursued embryological researches, or even read of them, cannot have failed to be impressed by that marvel of all marvels of an exceedingly minute portion of living matter, so small that a line would define it, passing by successive modifications into an organism so complex that a treatise is needed to describe it. Not only do the cells of the ovum and the spermatozoa originate and pass into a complex organism, reproducing the forms and features of its parents with their constitutional traits and peculiarities, but also the diseases, infirmities, tricks, and dispositions of generations and generations before. Consider what this implies. A microscopical cell, without the least trace of organs, not distinguishable from millions of other cells, nevertheless does contain within it the potentialities of a Newton, a Shakespeare, or a Napoleon. Each cell is *sui generis* a complete organism, and there can be no doubt that there is as much in

this small structure beyond the reach of our senses or the microscope as there is in the vast universe around us beyond the sweep of the telescope. Hence it is no gratuitous hypothesis that the cell does receive and retain impressions. Still, how is it that these impressions are transmitted to the cell's successors as a special quality? The new or daughter cell, we should always remember, is not a *product* of the parent cell, but in truth is the old cell elongated or branched. The old cell divides and makes two or three cells. The same cell and substances which at first received the impress are still present and continue to manifest it. Were this not so, owing to the ceaseless change transpiring in the organism, traces of experiences—structural changes—would disappear, and there could be no memory, evolution, or progress of any kind. The cells receive, retain, and transmit. They impart their *form* and substances to those which succeed them, and there is no gap but an elongation. That this is the case lies within the tangible experience of all in the formation of scar-tissue.

The original cells do not remain entirely and absolutely, but are constantly changing, and their places are being taken by others of their descendants. The injured cells retain and convey the mark of the injury to their successors for generations, and the "memory," modification, or molecular vibration is preserved and shown ever afterwards. Every kind of activity peculiar to living creatures or parts involves a change of structure, and the formation of the newly-generated tissue receives such an influence from the conditions under which it originates that all subsequent activity displays this impress. The same sum of external and internal environment, which once received a modification, now preserves it. The cell is but the expression of certain internal and external conditions of existence, and it alters with these.

Another and distinct class of data going to demonstrate this interpretation of the question of immunity, and that the factors of evolution and heredity are the true ones, is that found in connection with the clinical history, pathological anatomy, and sequence of the chronic or non-immunizing diseases. While it is true that the evidence derived from this source is of a negative character, still it is none the less convincing in its illustration of the import-

ance and efficiency of phagocytosis and heredity in arresting and preventing disease.

Upon what grounds can we explain the feature of persistence or chronicity of a disease? If the proteids are set free in the organism, as before described, in all germ diseases, why is it that the cells in chronic disease are never carried up to a condition of resistance which would enable them to successfully antagonize and protect themselves against future encroachments from their etiological agents? If the microorganisms are continually destroying the cells, and thereby setting free their constituents (as we know from the periodical fever and constitutional disturbances), which in turn cause the surviving cells to exercise their highest and best means of defence, how is it possible that they should ever become chronic, as in malaria, rheumatism, and other diseases? Why do the cells, when brought into direct contact with the microorganisms, never achieve an immunity, but succumb time after time? Manifestly, to discover the causes for this failure to accomplish immunity, we must understand the negative phase of the subject. As a fact, experience shows that every germ-disease selects and locates upon some particular seat or tissues from which it lives, flourishes, and proceeds to produce its deleterious effects upon the organism attacked. Another noticeable fact is, that the type, nature, and duration of a disorder are always influenced and controlled by the tissues attacked. This is true in so far that all germ-diseases may be divided into those which occupy the solid tissues and those which occupy the fluid tissue—the blood. Among those of the first class we find the exanthemata, such as measles, smallpox, whooping-cough, and others. In the second we have malaria, rheumatism, dengue, relapsing fever, erysipelas, and influenza. Following this division still further, we find that the disorders of the first are all, or nearly all, acute or self-limited and immunizing, while those of the second class are chronic and non-immunizing in character. Guided by these distinctions, we find that there is an anatomical and a physiological cause and basis for these discrepancies as to duration and consequence in germ-diseases. With these facts before us, we are warranted in assuming that these features are in some degree dependent upon the peculiarities of anatomical seat. It is

necessary, however, that we shall be able to refer this assumption to some standard of appeal, in order to show that it has other grounds than those of mere analogy or active imagination. Let us turn again to the life-history of the cell, endeavor to trace its genesis as an element in the blood, and to ascertain if it be possible to explain why a blood-disease has no power of limiting disease or of conferring immunity because the foregoing factors, as described, in the conditions necessary for adaptation, retention, and transmission of impressions are absent or imperfect in their use. To do this will be to establish the theory of Metschnikoff both positively and negatively, and to demonstrate its authenticity to be almost certain.

Physiology teaches that the white-blood cells, the amœboid, leucocyte, or phagocyte cells, have their origin severally in the spleen, the lymphatic structure, and the marrow of the long bones. It is from these sources that they arise, enter the current of the circulation, and finally pass out, under a number of circumstances, to become fixed cell-elements in the solid tissue. This being true, it is evident that the white-blood cell has an anomalous origin in that it is the product of a tissue histologically different and possessing no morphological or physiological resemblance to it. In this respect it occupies a position analogous to that of the ovum and the ovary, and to the spermatozoon and the testicle. In the illustrations given in the history, environment, and destiny of the cell, when capable of taking on modifications from influences in its media, we saw that certain conditions were necessary for its accomplishment, and that heredity or transmission depended upon certain conditions. In the chronic diseases the specific agents have been demonstrated in a number of instances to occupy the blood exclusively, and clinical history corroborates this. It is here that they exist, flourish, and produce their peculiar poisons which affect the organism. This being true, the only resisting or bactericidal agents or agencies, with which they are brought in contact, would be the white-blood cells and the blood-serum. Now, it is a fact that while the white-blood cells do multiply prodigiously and fight vigorously, as is evidenced by the chills, fevers, sweats, and general disturbance of the organism, still the germs multiply and persist, the disease becomes chronic, and phagocytosis is unavailing. The

cells or leucocytes multiply and destroy myriads and myriads of microorganisms, and yet the disease persists. How are we to reconcile this process with Metschnikoff's theory of phagocytosis and vital resistance being one and the same? It is because the second and essential factor of all superiority and permanent exemption is absent. The heredity and acclimating influences are absent in the white-blood cell as such. Its existence in the blood is of an ephemeral nature and it originates *de novo*, having neither pride of ancestry nor hope of posterity as a resisting or bactericidal agent in the blood. It can never inherit, acquire, or transmit a superiority, since the conditions of existence upon which these depend are entirely absent in its case. They live, flourish, and destroy as leucocytes in the blood; but in this transitory character they do not remain, but pass out into the solid tissue when they and their past experiences could never be of any possible service to those who come after them in the blood. The blood is to them now a foreign and remote locality, and under the conditions of their new environment has no possible influence upon them or they upon it. The blood-cell has the power of phagocytosis, but in a medium when everything is of a fleeting and transitory character, no accommodation can take place when the source of the supply is unlimited and the means of defence momentary in effects. Hence, the conditions of blood-diseases are such that no immunity can ever ensue, and the disease will persist unless the causes are all destroyed, or avoided, or artificial aid employed. *Having in this manner shown that it is the cells which acquire, retain, and transmit a superiority, and wherein they fail to do so, and the reason why,* we may assume that a new quota of data has been added to the theory of phagocytosis. Thus, the entire series of facts and their interpretation are in keeping with the laws of development, evolution, and heredity, and the phenomena and philosophy of immunity are apparently explicable through them. Life, which seeks its own continuance, tends to repair itself without our help. It mends its spider's-web when it has been torn; it reinstates in us the conditions of health, and itself heals the injuries inflicted upon it. The wisest part of us is that which is unconscious of itself, and what is most reasonable in man are those elements in him which do not reason.

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